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Report no.: V 82.361/220758

TWO-DAY STUDY TO THE RELATION BETWEEN POLYMERIC MDI CONCENTRATION VALUES OBTAINED BY A QCM-CASCADE, HPLC AND COLORIMETRY.

(final report)

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Authors : Drs L.M. Appelman [1] and Ing. F.G. Behlau [2]

At the request of : International Isocyanate Institute Inc., New Canaan, CT 06840, Conn., USA.

Project number : B 82-0758

Start of the study : September 8, 1982

End of the study : September 9, 1982

Date : November, 1982

1) Institute CIVO Toxicology and Nutrition TNO, Zeist, The Netherlands

2) Bayer AG, Sparte Polyurethane, Leverkusen, F.R.G.

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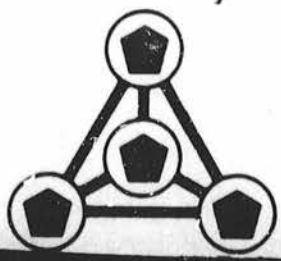

TWO-DAY STUDY INTO THE RELATION BETWEEN POLYMERIC MDI CONCENTRATION VALUES OBTAINED BY A QCM-CASCADE, HPLC AND COLORIMETRY

1. INTRODUCTION

At the request of the International Isocyanate Institute Inc. USA a research program is being performed to investigate the toxicological properties of inhaled polymeric MDI.

During a previous two-week inhalation study with polymeric MDI, carried out in the scope of this program, large, inconsistent differences were observed between concentration values obtained by the QCM-cascade and by HPLC analyses (see CIVO report no. V 82.308).
Since both methods of analyses should also be used during future studies with polymeric MDI, it was deemed necessary to perform an additional study to verify the relation between the results of both methods. The concentrations selected for this study were 0.2 and 1 mg/m^3 air, the same concentrations as will be examined during a three-month inhalation study.
Additionally, a colorimetric method for the determination of polymeric MDI in air was introduced.

2. MATERIAL AND METHODS

- Test material

A sample of polymeric MDI (Desmodur 44 V20) was received from Bayer AG, Leverkusen, FRG, in May, 1982. Desmodur 44 V20 is a viscous (η = 200 $\pm$ 40 mpas), dark brown liquid with the following composition as specified by Bayer AG:

NCO content	30 $\pm$ 2 % (w/w)
hydrolysable chlorine	$\leq$0.3 % "
total chlorine	$\leq$0.8 % "
chlorobenzenes	$\leq$0.015 % "
phenyl isocyanate	$\leq$0.005 % "
content of monomeric MDI	52 $\pm$ 3 % "
content of sediment	$\leq$0.01 % "

- Generation of the test atmospheres

The polymeric MDI aerosols were generated in a stainless steel/glass air nebuliser. A cyclone was placed behind the nebuliser to remove large particles to ensure that, upon entering the inhalation chamber, 95 % of the particles was smaller than 5 µm.

The total airflow through the chambers ranged from 45 to 54 m^3/hour. The concentrations of polymeric MDI in the test atmospheres were fixed at 0.2 and 1 mg/m^3 air.

- Test atmosphere control

The concentration of polymeric MDI in the two test atmospheres was determined by:

1) a Berkeley model C-1000A QCM Cascade Airborne Particle Size Analyzer.
2) Calculation from the monomeric MDI concentration determinated by HPLC.
3) Colorimetric dertermination of the total isocyanate content.

The frequency of sampling was according to the following scheme:

nominal concentration level	determination method					
	QCM		HPLC		color.	
(mg/m^3 air)	day 1	day 2	day 1	day 2	day 1	day 2
0.2	20	19	20	20	18	18
1	20	19	20	20	20	18

The particle size distribution in the polymeric MDI aerosol was determined five times.

All methods and analytical procedures, concerning the determination of polymeric MDI, except for the colorimetric method, are described in full detail in our report V 82.049.

The colorimetric method has been described in an addendum to this report.

3. RESULTS

The results of the concentration determinations of polymeric MDI both the individual and the mean data, are summarized in table 1. Particle size distributions are presented in table 2.

The results of table 1 showed that:

- The concentration data, obtained by HPLC, were uniform. On both days 19 out of 20 values determined in the 0.2 mg/m^3 atmosphere were within a range of the mean plus/minus two times the standard deviation, while at the level of 1.0 mg/m^3 even all values were within this range. The QCM-results and the colorimetry results showed a similar distribution.
- The variances, expressed as the coefficient of variance, within the concentration values, obtained with the different methods, were comparable (see table 1).
- The particle size distribution of the 0.2 mg/m^3 atmosphere and the 1 mg/m^3 atmosphere was about the same.

4. DISCUSSION

In previous studies with polymeric MDI aerosols differences were observed between results of concentration values obtained by HPLC at one side and gravimetry and colorimetry at the other.

In a Bayer report (Aufsatz et al.) it is mentioned that the polymeric MDI values obtained by HPLC in the 5 mg/m^3 range were smaller than those obtained by gravimetry; the differences between the results of both analytical methods became larger as the concentration became lower. Although in the present study the HPLC values were also lower than the gravimetric values, the differences between the results just became smaller as the concentration became lower.

During the preliminary studies (see CIVO report V 82.308) the ratio between results obtained by QCM-cascade and HPLC appeared to be 1.27 at a level of about 5 mg/m^3 air. The results of the present study showed a ratio of 0.50 for the 1 mg/m^3 atmosphere and a ratio of 0.90 for the 0.2 mg/m^3 atmosphere.

No explanation can be given for this discrepancy in results at this moment.

The results obtained by colorimetry are quite in agreement with those obtained by QCM. The ratio's between results obtained by the QCM-cascade and by colorimetry were 1.21 for the 5 mg/m^3 level, 1.10 for the 1 mg/m^3 level and 1.43 for the 0.2 mg/m^3 level.

From the data of the present study we recommend the photometric (colorimetric) method as a second, chemical method for the determination of polymeric MDI in the further planned inhalation toxicology studies.

5. REFERENCE

Aufsatz, M., H. Scheiter and J. Keller
Analytical methods to monitor aerosols of polymeric 4,4'-Diphenylmethane-diisocyanate (MDI) at low concentrations.
Bayer AG, Leverkusen, December 1981.

TABLE 1 - CONCENTRATIONS OF POLYMERIC MDI IN TEST ATMOSPHERES DETERMINED BY A QCM CASCADE (QCM), HPLC AND COLORIMETRY (COLOR.)

Nominal Concentration 0.2 mg/m^3 air

No	DAY 1			DAY 2		
	QCM	HPLC	COLOR.	QCM	HPLC	COLOR.
1	0.41	0.29	0.40	0.31	0.28	0.33
2	0.31	0.23	0.41	0.37	0.27	0.43
3	0.35	0.26	-	0.29	0.27	0.39
4	0.35	0.27	0.46	0.29	0.27	0.46
5	0.36	0.25	0.46	0.31	0.27	0.44
6	0.31	0.27	0.47	0.32	0.26	0.44
7	0.37	0.27	0.47	0.25	0.29	0.46
8	0.28	0.28	0.49	0.32	0.20	0.47
9	0.32	0.29	0.50	0.25	0.31	0.42
10	0.28	0.29	0.49	0.33	0.32	0.43
11	0.37	0.30	0.50	0.34	0.33	0.48
12	0.36	0.31	0.56	0.25	0.31	0.45
13	0.33	0.31	0.52	0.33	0.33	0.51
14	0.35	0.31	0.54	0.28	0.33	0.47
15	0.33	0.31	0.55	0.32	0.31	0.34
16	0.37	0.31	0.50	0.35	0.29	0.41
17	0.34	0.30	0.53	0.34	0.33	0.49
18	0.45	0.30	-	0.29	0.30	0.53
19	0.28	0.32	0.54	0.28	0.30	-
20	0.27	0.32	0.50		0.30	-
Mean	0.34	0.29	0.49	0.31	0.29	0.44
SD.*	0.045	0.025	0.04	0.035	0.032	0.05
CV**	13.2	8.6	8.2	11.3	11.0	11.4

* SD = Standard Deviation
**CV = Coëfficiënt of Variance

TABLE 1 - CONTINUED 1.

Normal Concentration 1 mg/m^3 air

No	DAY 1			DAY 2		
	QCM	HPLC	COLOR.	QCM	HPLC	COLOR.
1	1.22	0.67	1.43	1.13	0.62	1.30
2	2.33	0.70	1.56	1.56	0.62	1.50
3	1.41	0.73	1.73	0.76	0.44	0.88
4	1.37	0.60	1.56	1.16	0.40	0.88
5	1.33	0.54	1.41	0.80	0.38	0.96
6	1.19	0.57	1.46	0.70	0.36	0.90
7	1.13	0.56	1.29	0.89	0.34	0.81
8	1.13	0.59	1.49	1.13	0.31	0.71
9	1.03	0.51	1.26	0.79	0.28	0.79
10	1.12	0.54	1.27	0.68	0.42	0.68
11	1.32	0.63	1.37	0.73	0.49	1.17
12	1.66	0.65	1.29	0.93	0.57	1.34
13	1.13	0.72	1.43	0.96	0.59	1.29
14	1.29	0.70	1.41	1.24	0.59	1.33
15	1.29	0.67	1.43	0.93	0.60	1.43
16	1.29	0.72	1.51	1.04	0.69	1.27
17	1.11	0.72	1.03	0.85	0.68	1.48
18	1.49	0.75	1.45	0.98	0.65	1.17
19	1.13	0.80	1.59	1.37	0.67	-
20	2.15	0.72	1.33	-	0.63	-
Mean	1.36	0.65	1.42	0.96	0.52	1.11
SD*	0.34	0.08	0.15	0.25	0.14	0.28
CV**	25	12.3	10.6	26.0	26.9	25.2

* SD = Standard Deviation
** CV = Coëfficiënt of Variance

TABLE 2 - PARTICLE SIZE DISTRIBUTION OF POLYMERIC MDI AEROSOLS

Dose level	Aerodynamic diameter D50 (nm)	Distribution (%) in sample 1	2	3	4	5
	22.6	0	0	0	0	0
	10.9	0	6	4.6	0	0
	6.4	6.9	6.3	9.9	9.2	8.1
	3.3	5.3	9.8	15.2	7.1	18.7
0.2 mg/m^3	1.80	13.8	12.7	19.8	13.9	16.7
	1	55.7	54.9	37.3	54.9	48.2
	0.60	11.1	10.3	13.3	14.9	8.7
	0.37	7.4	0	0	0	0
	0.20	0	0	0	0	0
	0.12	0	0	0	0	0
MMAD[1] = 2.4 µm						
σg[2] = 2 µm						
	22.6	0	0	0	0	0
	10.9	0	0	0	0	0
	6.4	0	4.7	0	3.3	0
	3.3	8.5	7.3	18.2	5.1	2.3
1 mg/m^3	1.80	46.9	47.3	47.6	43.2	47.0
	1	23.8	23.0	25.7	32.3	31.1
	0.60	14.8	17.8	8.5	12.5	13.0
	0.37	3.0	0	0	3.6	4.9
	0.20	3.1	0	0	0	1.7
	0.12	0	0	0	0	0
MMAD = 1.7 µm						
σg = 2 µm						

1) MMAD = Mass Median Aerodynamic Diameter
2) σg = Geometrical Standard Deviation

ADDENDUM TO REPORT NO. V 82.361

TWO-DAY STUDY INTO THE RELATION BETWEEN POLYMERIC MDI CONCENTRATION VALUES OBTAINED BY A QCM-CASCADE, HPLC AND COLORIMETRY.

Analytical method for the determination of Polymeric MDI in air.

Author: Ing F.G. Behlau.

6. CALCULATION

The concentr tion of polymeric MDI is calculated as follows:

$$C_a \quad \frac{A_2 \times V_1 \times 1000}{F \times d \times V_2}$$

C_a = concentration of polymeric MDI in the air in mg/m^3

A2 = absorbency at 555 nm

F = standard factor for 1 mg of polymeric MDI dissolved in 1 ml

d = path length in cm

V1 = volume of measuring solution in ml in total 23 ml (5 ml of solution mixed with water and reagents to give 23 ml)

V2 = air sample volume in litres.

DETERMINATION OF POLYMERIC MDI IN AIR - COLORIMETRIC METHOD

1. PRINCIPLE OF THE METHOD

Air is drawn through a washing bottle containing 5 ml of an absorber solution with a flowrate of 1.5 l/min. MDI is absorbed and hydrolyzed to the corresponding amines. After diazotation and coupling with 1-(N-naphtyl)-ethylenediamide the absorbency of the solution is determined spectrophotometrically against blanks.

2. APPARATUS

2.1 Air sampling device.

The inlet of the washing bottle (figure 1) is connected with the chamber. The outlet is fitted to an air sampler (e.g. type Rotheroe and Mitchell).

2.2 Spectrophotometer.

Zeiss DMR 21 spectrophotometer or similar equipment.

3. REAGENTS

3.1 Solution of concentrated sulfuric acid in dimethylsulfoxide (5/95 v/v).

3.2 Solution of 1.5 g of $NaNO_2$ and 3.6 g of KBr in 100 ml of water.

3.3 Solution of 15 g of sulfamic acid (NH_2-SO_3H) in 100 ml of water.

3.4 Solution of 1 g of 1-(N-naphthyl)-ethylenediamine and 2 ml of 1 N-hydrochloric acid in 100 ml water.

3.5 2 N-hydrochloric acid.

4. METHOD

4.1 Air sampling.

The washing bottle is filled with 5 ml of solution 3.1. The inlet of the bottle is connected with the inhalation chamber. Air is drawn through the absorber solution with a flowrate of 1.5 l/min for approx. 10 minutes.

4.2 Analytical procedure.

4.2.1 Add 5 ml of water to the washing bottle. Allow the solution to cool down for 15 minutes.

4.2.2 Add 1 ml of solution 3.2, wait 5 minutes.

4.2.3 Add 1 ml of solution 3.3, wait 5 minutes.

4.2.4 Add 1 ml of solution 3.4, wait 10 minutes, shake solution frequently for release of nitrogen.

4.2.5 Add 10 ml of 2 N-hydrochloric acid.

4.2.6 Leave the solution for 60 $\pm$ 15 minutes. Run a spectrum of the solution and a blank in the range of 830 nm to 520 nm. Measure the absorbency (A) in the maximum of absorption at 555 nm.

5. CALIBRATION

Follow procedure with standard solution.
Calculation of standard factor F:

$$F = \frac{Al \times V}{w \times d}$$

Al = absorbency at 555 nm
V = volume of measuring solution
w = polymeric MDI in the measuring solution in mg
d = path length in cm

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